IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

STEPHEN WENDELL and LISA WENDELL, as successors in interest to MAXX WENDELL, deceased,

Plaintiffs,

v.

JOHNSON & JOHNSON; CENTOCOR, INC.; ABBOTT LABORATORIES; SMITHKLINE BEECHAM d/b/a GLAXOSMITHKLINE; TEVA PHARMACEUTICALS USA; GATE PHARMACEUTICALS, a division of TEVA PHARMACEUTICALS USA; and PAR PHARMACEUTICAL, INC.,

Defendants.
_____/

No. C 09-04124 CW

ORDER DENYING CENTOCOR AND JOHNSON AND JOHNSON'S MOTION FOR SUMMARY JUDGMENT, GRANTING PLAINTIFFS' MOTION FOR RECONSIDERATION, DENYING ABBOTT, TEVA AND PAR'S MOTIONS FOR SUMMARY JUDGMENT, AND GRANTING GSK'S MOTION FOR SUMMARY JUDGMENT

This is a pharmaceutical products liability case in which Plaintiffs Stephen and Lisa Wendell have sued as successors-in-interest to their deceased son Maxx Wendell. Plaintiffs have brought strict liability and negligence claims alleging that Defendants failed to provide adequate warnings of the risk of hepatosplenic T-cell lymphoma presented by certain drugs--Humira, Remicade and 6-mercaptopurine (6-MP).[1]

On March 2, 2011, GlaxoSmithKline LLC (GSK)[2] moved for summary judgment, but the Court denied the motion without prejudice pursuant to Federal Rule of Civil Procedure 56(d). On

[1] 6-mercaptopurine is also known as mercaptopurine and Purinethol.

[2] GSK was formerly known as and erroneously served and sued in this action as SmithKline Beecham d/b/a GlaxoSmithKline.

June 23, 2011, the Court approved the parties' stipulation to vacate all case management deadlines and stay discovery until after the parties' mediation or the ruling on Defendants' motions for summary judgment, whichever occurs later, and at that time to determine a proposed schedule for the remainder of the case.

Subsequently, Defendants Abbott Laboratories, GSK, TEVA Pharmaceuticals USA, which includes Gate Pharmaceuticals, and PAR Pharmaceutical, Inc., moved for summary judgment on the grounds that Plaintiffs lacked evidence to establish proximate causation. Docket Nos. 177, 179, 183 and 185. Abbott manufactures, markets, distributes and sells Humira. TEVA distributes 6-MP products that have been resold in California and has marketed and advertised the product under the brand name Purinethol. GSK manufactured, labeled, packaged and marketed Purinethol in the United States prior to July 2003. PAR distributes 6-MP in California. These Defendants argued that Plaintiffs lacked evidence to show that a different warning would have changed the treating physician's decision to prescribe Humira and 6-MP to Maxx. Defendants Johnson & Johnson and its wholly owned subsidiary, Centocor, Inc., which manufactured, marketed, sold and distributed Remicade, did not file motions for summary judgment at that time. On December 15, 2011, the Court granted summary judgment in favor of Abbott, GSK, TEVA and PAR.

After the Court's ruling, Johnson & Johnson and Centocor moved for summary judgment, arguing that Plaintiffs lacked evidence to establish that a failure to warn of the risk associated with Remicade caused harm to Maxx. Docket No. 205. Johnson and Johnson also argued that it was not involved with the

research, production, marketing or distribution of the drug. After briefing on the second motion for summary judgment was completed, Plaintiffs moved for leave to file a motion for reconsideration of the Court's December 15, 2011 order. Docket No. 220. Plaintiffs argued that new evidence presented in connection with the second motion for summary judgment warranted reconsideration. Abbott, GSK and TEVA opposed the request for reconsideration. On April 12, 2012, the Court granted Plaintiffs' request for leave to file a motion for reconsideration and allowed Defendants to file additional briefing.

Having considered all of the parties' submissions and oral argument, the Court denies Centocor and Johnson and Johnson's motion for summary judgment. In addition, the Court grants Plaintiffs' motion for reconsideration of its December 15, 2011 order and, upon reconsideration, denies Abbott's, TEVA's and PAR's motions for summary judgment. The Court grants GSK's March 2, 2011 motion for summary judgment on the grounds that it discontinued its sales of Purinethol in 2003, before its risks were known.

BACKGROUND

In the fall of 1998, Maxx was diagnosed with inflammatory bowel disease (IBD), and began receiving treatment from Dr. Edward Rich, a pediatric gastroenterologist at Kaiser Permanente in San Francisco. Rich Dep. at 50:5-10, 59:22-60:1, 74:23-25.[3]

[3] The complete transcript of the deposition is located at Docket No. 199.

Dr. Rich testified that it was not his "regular practice to look at drug labeling." Id. at 192:6-7. He received information on medications from multiple sources, including conferences and large meetings with pediatric gastroenterologists and adult IBD specialists, as well as smaller regional meetings and dinner meetings with these colleagues. Id. at 251:5-252:2. Dr. Rich also gained knowledge about therapies from discussions with other professionals in the field, articles and occasional meetings with drug representatives. Id. at 192:7-14. He explained, "Generally I'm looking at drug labeling or the PDR in medicines that I'm less familiar with."

With respect to the impact of drug labeling on his decisions regarding treatment, Dr. Rich testified, "Drug labeling is sometimes something I rely on when making decisions on drug use for patients." Id. at 190:21-23. He stated, "When I read the labeling, it's one of the things that is part of my decision-making process." Id. at 191:20-22. Dr. Rich could not remember whether he ever relied on labeling information for 6-MP before prescribing it to patients. Id. at 282:2-283:2.

In June 1999, Maxx began taking 6-MP, an immunosuppressive medication. Id. at 105:14-15. Dr. Rich prescribed varying dosages of 6-MP, while attempting to wean Maxx from Prednisone, a steroid. However, as of May 2002, Maxx was still taking Prednisone and 6-MP. Id. at 117:4-11.

At the time Dr. Rich prescribed 6-MP he was aware of a paper reporting the occurrence of lymphoma in adults taking the drug. Id. at 89:12-90:17. According to Dr. Rich, the frequency of lymphoma occurrences reported in the study was one in one hundred

adult patients taking 6-MP. Id. at 89:23-90:4. Dr. Rich found this "significant," prompting him to warn patients of a "small but non-zero increased risk of serious infections or malignancies" when discussing 6-MP treatment. Id. at 89:2-90:17. Dr. Rich testified that he may or may not have included the word "lymphoma" when providing the warning. Id. at 89:7-12.

At an appointment with Maxx on May 8, 2002, Dr. Rich discussed in detail prescribing Remicade. Id. at 117:4-118:1. Again, the goal in changing Maxx's medication at this time was to take him off steroids. Id. at 151:17-152:9. On July 10, 2002, Maxx received his first infusion of Remicade. Id. at 147:24-148:16. Maxx received infusions of Remicade approximately every three months thereafter, in combination with 6-MP. Id. at 155:4-12, 157:9, 170:12-21.

Dr. Rich considered Remicade, as well as Humira, part of a class of anti-tumor necrosis factor (TNF) drugs, also known as TNF inhibitors. Id. at 175:10-14, 176:9-17, 264:24-25, 265:2-3. He testified that he "virtually always" informed his patients of a "nonzero increased risk" of serious infections and malignancies related to "immunosuppressives and anti-tumor necrosis factor drugs." Id. at 123:6-10. According to Dr. Rich, at a point in time he could not recall, he became aware of a study involving approximately 700 patients on Remicade therapy, a majority of whom had rheumatoid arthritis and a minority of whom had Crohn's disease. Id. at 125:13-19. The study reported incidents of serious infections and malignancies, including lymphomas, within that patient population. Id. at 125:20-126:1. This is consistent with an entry regarding Remicade in the 2002 Physicians' Desk

Reference, which included mention of a clinical study involving 771 patients, seven of whom developed new or recurrent malignancies, including lymphoma. Id. at 133:2-12. However, the PDR also stated that "the observed rates and incidents [of these malignancies] were similar to those expected for the population." Id. at 133:10-12. According to Dr. Rich, in 2002 there were no reports on the risk of therapies combining Remicade and 6-MP. Id. at 132:10-12.

In February 2005, the first case report was published of an IBD patient with hepatosplenic T-cell lymphoma who had received immunosuppressive therapy in combination with Remicade.[4] Declaration of Kevin Haverty in support of Plaintiffs' Opposition, Ex. 4, Rosh Report, at 5. Hepatosplenic T-cell lymphoma is a rare, incurable, aggressive cancer that is nearly always fatal. Id. at 2-3. Of eight cases of young patients diagnosed with hepatosplenic T-cell lymphoma reported to the federal Food and Drug Administration (FDA), six died. Defendant Abbott Labs, TEVA and Par's Further Opposition to Plaintiffs' Mot. for Reconsideration, Ex. 2, FDA Short Communication, at 265. Each of

[4] The first case report was "Hepatosplenic T-cell lymphoma in an adolescent patient after immunomodular and biologic therapy for Crohn's disease," authored by Thayu M., Markowitz J.E., Mamula P., et al. (Thayu Report), and published in the Journal of Pediatric Gastroenterology and Nutrition. The Thayu Report refers to infliximab, another name for Remicade, see e.g., Jones Affidavit, Ex. G, May 2006 Remicade Package Insert, at 1, and describes immunomodulatory and biologic therapy as treatment combining 6-MP and Remicade. A May 2007 report entitled, "Hepatosplenic T-cell lymphoma in adolescents and young adults with Crohn's disease: A cautionary tale?," authored by Rosh J.R., Gross T., Mamula P., Griffiths A. and Hymans J. (Rosh Report), referred to the Thayu Report as the first such case report. Haverty Dec., Ex. 4 at 5.

the patients succumbed to the cancer within a year or less from the time of diagnosis. Id. at 266.

In November 2005, Centocor submitted to the FDA a supplemental Biologic License Application (sBLA) seeking approval of a new use of Remicade for treatment of pediatric Crohn's disease.

Also in November 2005, Dr. Rich began to consider discontinuing Maxx's Remicade treatment and discussed Humira with him. Id. at 170:24-173:5. Dr. Rich testified that in "late 2005" he became aware of a "complication" associated with Remicade, namely the occurrence of hepatosplenic T-cell lymphoma in adolescent and young adult patients taking Remicade with 6-MP. Id. at 204:21-205:22, 215:3-4.

In his deposition, Dr. Rich was not asked directly about the source of his knowledge about the complication, but he testified,

> I knew this information before the black box warning or messaging from the patient (verbatim). I was aware of literature as it evolved. This is a very important part of our treatment. And was aware from many sources when cases first got--were first reported, came to my attention. I believe that was sometime in 2005. I can't tell you when . . .
>
> I can't remember exactly the time course of what I learned and where. At some point I became aware of cases of hepatocellular [sic] T-cell lymphoma in young males on combination therapy of Remicade and immunosuppressive therapy. And at some point, there was a report. I can't--I don't remember if it was first at a meeting--I didn't attend the meeting, if that was true--or if it was an abstract or if it was just a case report of a number of patients.
>
> The number in my head is something like six patients with this rare or uncommon lymphoma. And then at some point there was an article on this, I believe. At first it might have been a report and then an article,

> but I can't exactly be sure. And when the article came out it was six to eight patients, and this was before the black box warning came out.

Id. at 205:15-23; 206:12-207:5.

When asked whether any doctor had discussed a case of hepatosplenic T-cell lymphoma with him, Dr. Rich testified that he may have learned of such a case from a colleague in the East Bay and a doctor from Atlanta. Id. at 29:24-32:5. Dr. Rich did not recall the specific date or month when the conversations occurred. He testified repeatedly that he did not remember when his informal discussion with the Atlanta-based physician occurred. At one point, he stated that the discussion may have occurred in the late 1990s, but then retracted this and testified that he learned of the case "when patients with side effects were being reported, but not many, so that would be approximately the mid-2000s." Id. at 32:21-35:6. Dr. Rich also testified that when Maxx's case was discussed with his regional pediatric gastroenterology group, which met quarterly, a pediatric gastroenterologist from the East Bay may have mentioned such a case. Id. at 15:5-25.

Maxx received an infusion of Remicade in November 2005 and then his final dose of Remicade in March 2006. Id. at 182:15-14; 197:16-199:7. Between February 2005 and February 2007, nine cases of hepatosplenic T-cell lymphoma in IBD patients receiving

combination therapy were confirmed, in addition to Thayu's case.[5] Rosh Report at 5.

In April 2006, as part of Centocor's sBLA and the FDA's review of the application, a safety signal was identified for hepatosplenic T-cell lymphoma. Affidavit of Stella Jones at ¶ 11. As defined by the FDA in a guidance document, a safety signal "refers to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use." Id. at ¶ 12. Safety signals may arise from post-marketing data and other sources, and even a single well-documented case report can be viewed as a signal. Id. Centocor's submission did not reveal the nature of the safety signal. In Abbott, TEVA and PAR's further opposition to Plaintiffs' motion for reconsideration,[6] they state that, in addition to the first case report published in February 2005, there were five cases reported to the FDA's Adverse Event Reporting System (AERS) through May 2006, when Centocor added the black-box warning to the Remicade label and distributed a "Dear Healthcare Provider" letter to physicians.

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[5] The Rosh Report examined ten incidents of hepatosplenic T-cell lymphoma in young patients receiving Remicade in combination with 6-MP or azathioprine (AZA), the parent compound of 6-MP. Rosh Report at 2, 6. The Rosh Report cited Centocor data as well as an FDA "Short Communication" authored by researchers from the Center for Drug Evaluation and Research, a part of the federal agency. The Short Communication was published in February 2007 in the Journal of Pediatric Gastroenterology and Nutrition. Defendants Abbott, TEVA and Par's Further Opposition to Plaintiffs' Mot. for Reconsideration, Ex. 2.

[6] Centocor and Johnson & Johnson, as well as GSK, joined the arguments made in this opposition brief. Docket Nos. 229 and 230.

In May 2006, the FDA approved the new use of Remicade for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Jones Affidavit at ¶ 14. However, the FDA also required the addition of the following black box warning:

> RARE POSTMARKETING CASES OF HEPATOSPLENIC T-CELL LYMPHOMA HAVE BEEN REPORTED IN ADOLESCENT AND YOUNG ADULT PATIENTS WITH CROHN'S DISEASE TREATED WITH REMICADE. THIS TYPE OF T-CELL LYMPHOMA HAS A VERY AGGRESSIVE DISEASE COURSE AND IS USUALLY FATAL. ALL OF THESE HEPATOSPLENIC T-CELL LYMPHOMAS WITH REMICADE HAVE OCCURRED IN PATIENTS ON CONCOMITANT TREATMENT WITH AZATHIOPRINE OR 6-MERCAPTOPURINE.

Haverty Dec., Ex. 3.

Dr. Rich testified that he would have received this black box warning in the form of a letter or other notification at about the time it was issued. Rich Dep. at 214:23-215:3.

Also in May 2006, Maxx underwent a colonoscopy that revealed no signs of IBD. Id. at 198:1-199:14. According to Dr. Rich, a decision to discontinue Remicade or use an alternative medication would have been made at the time of the colonoscopy, based on the results of the examination. Id. at 172:10-12. Maxx received no further infusions of Remicade.

As of October 5, 2006, the AERS had received notice of eight young patients with Crohn's Disease and ulcerative colitis who received Remicade with concomitant immunosuppressant therapy, including 6-MP in some cases, and developed hepatosplenic T-cell lymphoma. Abbott, TEVA and Par's Further Opposition to Plaintiffs' Mot. for Reconsideration, Ex. 2, FDA Short Communication.

By November 2006, Maxx experienced a relapse. On November 22, 2006, he received his first prescription for Humira, taking the drug in combination with 6-MP. Id. at 217:14-16. Dr. Rich testified that he first treated patients with Humira in early 2005 or 2006 when two sixteen-year-old female patients with IBD received the drug. Id. at 193:3-7; 173:19-25. Dr. Aileen Dillon, a rheumatologist, wrote Maxx's first prescription for Humira because, when Humira was first placed on the Kaiser formulary, it was placed under limited release, only through rheumatologists. Id. at 217:14-218:6. Dr. Rich testified that when he first began prescribing Humira to his patients, he warned them of a "nonzero but increased risk of serious infections and malignancies." Id. at 193:23-194:11. His awareness of this risk was based on literature he had reviewed and discussions he had had with other physicians. Id. at 194:12-18.

When asked why he did not treat Maxx with Remicade in November 2006, Dr. Rich responded,

> So in November '06, we had been aware for some time of complication of hepatosplenic T-cell lymphoma, so that would have been part of my discussion with the family. Ease of therapy is always a discussion with Humira versus Remicade.

Id. at 218:13-23. Dr. Rich explained that Humira may be administered by the patient or a family member at home through subcutaneous injections, while Remicade requires a patient to visit a facility for two to three hour infusions. Id. at 174:15-19, 267:5-23.

When asked whether he opted for Humira because of the black box warning concerning Remicade, Dr. Rich testified, "I think that

the concern of hepatosplenic T-cell lymphoma would have been part of my discussion with the family and it would have been part of my thinking about the use of this disease (verbatim)." Id. at 219:16-22. Dr. Rich did not recall any similar warning regarding Humira's use in combination with 6-MP and hepatosplenic T-cell lymphoma. Id. at 219:23-220:2. Dr. Rich did not state that he would not have prescribed Humira in November 2006, had there been a black box warning or similar alert regarding the use of Humira, alone or in combination with 6-MP, and the occurrence of hepatosplenic T-cell lymphoma. Maxx's mother, Lisa Wendell, testified that Dr. Rich never informed her of the black box warning concerning Remicade, but told her that Humira had a better safety profile, in addition to being easier to administer. Haverty Dec., Lisa Wendell Dep. at 77:4-13.

In deposition, Dr. Rich was asked whether his drug recommendation was informed by the fact that Remicade had a black box warning about a rare, aggressive cancer, while Humira did not. Dr. Rich responded,

> I don't think the black box would have been a primary driving point in the use of medicine, just as FDA indication or not is not a driving point, as FDA doesn't indicate very much of anything in pediatrics.

Id. at 220:1-15.

Later, Dr. Rich was asked again whether information that he had about the cases of hepatosplenic T-cell lymphoma associated with Remicade and 6-MP combination use informed in any way his

recommendation that Maxx start Humira in November 2006. He answered,

> The occurrence of hepatosplenic T-cell lymphomas and the information and knowledge about that would have been part of many things that would have gone into my own thinking on how to use this--these medications and my discussion with the patients on how to use these medications.

Id. at 225:7-113.

In addressing whether all anti-TNF drugs carry the same risks, Dr. Rich testified that Humira was "entirely humanized," whereas Remicade was "75 percent humanized and 25 percent mouse." Id. at 194:24-25. Dr. Rich engaged in the following exchange with counsel,

> A: So I presented [anti-TNF] medications always as having an increased but nonzero increased risk. And if I was asked by a patient, "Why do you use one versus the other," or why we were considering Humira, it may have come up in discussions that Humira was fully humanized and may have--my statement would have --would have been, "It may have a better safety profile."
>
> Q: What was the basis of your thinking that it may have a better safety profile?
>
> A: That it was fully humanized.
>
> Q: What--
>
> A: That there are allergy side effects to these medicines.
>
> Q: Okay. Other than allergies, did the fact that Humira was fully humanized, monoclonal antibody, as opposed to Remicade, affect, in your mind, the risk of malignancies?
>
> A: I can't recall whether I thought that or not. The fact that there--I'm not an immunologist, and I'm not sure they can answer that question. But the fact that there is no mouse suggests that it might have been a consideration in my thinking, that it's a possibility.

Id. at 195:13-196:12.

When asked if he had "an opinion about whether or not Humira had a better safety profile than Remicade for use in combination therapy with 6-MP" with respect to the risk of hepatosplenic T-cell lymphoma, Dr. Rich responded,

> I don't believe I had an--an opinion. There was a--had been a thought, as I said, that Remicade may--Humira, excuse me, may have a better safety profile. And I don't remember what I thought or didn't think or knew about cases in November of '06. But I don't believe there had been cases reported at that time of patients with Humira developing hepatosplenic T-cell lymphoma. So it would have been a possibility in my mind that it had a better safety profile, and I would have said that to a patient.

Id. at 226:21-227:7.

Based on Dr. Rich's recommendation, Maxx took Humira for at least eight months. In mid-July 2007, Maxx was diagnosed with hepatosplenic T-cell lymphoma. In December 2007, he passed away.

As noted earlier, in February 2007, the FDA published a Short Communication in the Journal of Pediatric Gastroenterology and Nutrition, authored by researchers from the agency's Center for Drug Evaluation and Research. Defendants Abbott, TEVA and Par's Further Opposition to Plaintiffs' Mot. for Reconsideration, Ex. 2. The Short Communication reported that, as of October 5, 2006, the AERS had received notice of eight young patients with Crohn's Disease and ulcerative colitis who received Remicade with concomitant immunosuppressant therapy, including 6-MP in some cases, and developed hepatosplenic T-cell lymphoma.

In May 2007, as previously mentioned, the Rosh Report was published. It examined ten incidents of hepatosplenic T-cell

lymphoma in young patients receiving 6-MP or AZA in combination with Remicade.

During 2007 Dr. Rich continued to treat patients using therapies combining anti-TNF drugs with 6-MP, although he could not recall whether the "combination therapy" consisted of 6-MP combined with Remicade or 6-MP combined with Humira or both. Rich Dep. at 208:11-209:5. Most likely in 2008, Dr. Rich switched to using "mono-therapy," treating patients with an anti-TNF drug alone without concomitant use of 6-MP. Id. at 208:16-17, 288:13-16. Maxx's case played an "important role" in influencing Dr. Rich's decision to use monotherapy as opposed to combination therapy. Id. at 230:16-20. Dr. Rich reported that the majority of practitioners, including many pediatric gastroenterologists, use combination therapy, although that is no longer his practice. Id. at 230:12-15.

LEGAL STANDARD

Summary judgment is properly granted when no genuine and disputed issues of material fact remain, and when, viewing the evidence most favorably to the non-moving party, the movant is clearly entitled to prevail as a matter of law. Fed. R. Civ. P. 56. Celotex Corp v. Catrett, 477 U.S. 317, 322-23 (1986); Eisenberg v. Ins. Co. of N. Am., 815 F.2d 1285, 1289 (9th Cir. 1987). The court must draw all reasonable inferences in favor of the party against whom summary judgment is sought. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587 (1986); Intel Corp. v. Hartford Accident & Indem. Co., 952 F.2d 1551, 1558 (9th Cir. 1991).

Material facts which would preclude entry of summary judgment are those which, under applicable substantive law, may affect the outcome of the case. The substantive law will identify which facts are material. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986).

DISCUSSION

I. Centocor and Johnson & Johnson's Motion for Summary Judgment

Under the learned intermediary doctrine, a manufacturer of a prescription drug is obliged to warn doctors, not patients, of potential side-effects associated with its pharmaceutical products. Carlin v. Superior Court, 13 Cal. 4th 1104, 1116 (1996). A manufacturer of prescription drugs discharges its duty to warn if it provides an adequate warning to the physician about any known or reasonably knowable dangerous side effects of a medicine, regardless of whether the warning reaches the patient. Carlin, 13 Cal. 4th at 1116-17. A plaintiff asserting causes of action for failure to warn must prove not only that no warning was provided or that the warning was inadequate, but also that the inadequacy or absence of a warning caused the plaintiff's injury. Plummer v. Lederle Laboratories, 819 F.2d 349, 358 (2d Cir. 1987) (applying California law). Under Motus v. Pfizer, Inc., 358 F.3d 659, 661 (9th Cir. 2004), "a product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician."

Centocor asserts that it is entitled to summary judgment because its warnings concerning Remicade were adequate in that the labels had long advised of the risk of lymphomas associated with

the drug. However, Plaintiffs' claim is based on Centocor's alleged failure to warn of the risk of hepatosplenic T-cell lymphoma, a rare type of lymphoma that is nearly always fatal. Furthermore, pursuant to the parties' stipulation, the summary judgment motions at this time are to address the issue of proximate causation. If the case is not disposed of on the issue of proximate causation, discovery and litigation on other issues, such as the adequacy of the labeling will proceed. Plaintiffs correctly note that as a result of the discovery stay they have been unable to depose Dr. Stella Jones, who submitted an affidavit concerning Remicade label changes. Thus, they have been unable to uncover what was known to Defendants about lymphomas at the time labels were issued. The purported adequacy of the labeling, at this point in time, is not a basis for granting summary judgment in favor of Centocor.

Centocor also argues that Plaintiffs cannot establish proximate causation because Dr. Rich was already aware, as of "late 2005," of the occurrence of hepatosplenic T-cell lymphoma in adolescent and young adult patients taking Remicade with 6-MP, but he continued to prescribe the medications together. Plaintiffs point to medical literature to dispute Dr. Rich's testimony on this point. Dr. Rich's explanation of the course of events as he learned of the risk of hepatosplenic T-cell lymphoma could support a finding that he did not learn of it until after late 2005, perhaps not until the black box warning in May 2006. Dr. Rich stated that he could not remember the exact time and circumstances when he learned of hepatosplenic T-cell lymphoma occurring in young males receiving combination therapy. He testified that in

late 2005 he became aware of such cases, plural. Dr. Rich stated that he did not recall if he first learned of the cases at a meeting, but if the cases were reported at a meeting, he was not in attendance. He recalled learning of approximately six incidents from a case report or abstract, followed by further reporting in an article. However, the Rosh Report indicates that, as of February 2005, there was only one case report, the Thayu Report, in the medical literature concerning such an incident.

It is not disputed that five additional cases were reported to the FDA through AERS by May 2006. Yet, there is insufficient evidence for a jury to infer reasonably that Dr. Rich learned of the five cases before Maxx's last dose of Remicade in March 2006. Dr. Rich testified that he learned about drug therapies from a variety of sources. However, he did not state that he received information about the AERS-reported cases from any large meetings, conferences and smaller gatherings with colleagues. He testified that he may have learned of two cases from discussions with physicians based in the East Bay and Atlanta. However, Dr. Rich evidently learned of the case from the East Bay physician after Maxx was diagnosed with hepatosplenic T-cell lymphoma and discussed such a case with the physician from Atlanta in the "mid-2000s."

It was not until February 2007 and May 2007, respectively, that the FDA Short Communication and the Rosh Report were published. The Short Communication relayed that the AERS had received notice of eight young patients receiving combination therapy who developed hepatosplenic T-cell lymphoma. The Rosh Report addressed ten such cases. Defendants have not pointed to a

publication earlier than February 2007 discussing the occurrence of hepatosplenic T-cell lymphoma in multiple young patients receiving combination therapy. Dr. Rich's description of his knowledge is consistent with the February 2007 publication of FDA's Short Communication, followed by the Rosh Report, published in May 2007.

In sum, Plaintiffs have pointed to evidence that shows a paucity of published information in 2005 and early 2006 concerning the risk of hepatosplenic T-cell lymphoma for patients receiving Remicade and 6-MP concurrently; Dr. Rich's poor memory as to when he learned of the risk; and the chronology of relevant publications in 2007, which reconciles with his description of how he learned of such cases. Thus, the evidence is sufficient to raise a material dispute of fact as to whether Dr. Rich was aware of the risk before Maxx's last dose of Remicade and 6-MP in March 2006 and the May 2006 issuance of the black box warning.

Centocor seeks summary judgment on the grounds that any failure to warn earlier did not cause harm to Maxx because Dr. Rich was already aware of the risk. However, because of the evidence from which it can be inferred that Dr. Rich learned of the risk no earlier than May 2006, there is a material dispute of fact as to whether Dr. Rich knew of the risk in late 2005.

Moreover, there is evidence indicating that, had Dr. Rich known earlier of the risk of hepatosplenic T-cell lymphoma, he would have decided against prescribing Remicade in combination with 6-MP. Dr. Rich's testimony could be understood to imply that his awareness of the risk of hepatosplenic T-cell lymphoma in connection with Remicade and 6-MP influenced his decision to

prescribe Humira, rather than Remicade, when Maxx experienced a relapse in November 2006. Further, Dr. Rich now prescribes monotherapy only, after Maxx developed hepatosplenic T-cell lymphoma while receiving combination therapy and after Dr. Rich learned of the reports of the disease in young patients receiving combination therapy. This raises a question of fact as to whether an earlier warning of the risk would have influenced Dr. Rich to change his prescribed treatment for Maxx.

This case is distinguishable from Plummer. In Plummer, the Second Circuit, applying California law, found that judgment should have been entered for the defendant, because the physician knew of the risk for which the plaintiff sought a warning. The court concluded that "no harm could have been caused by failure to warn of a risk already known." 819 F.2d at 359. In contrast to Plummer, there is a dispute of fact as to whether Dr. Rich already knew of the risk of hepatosplenic T-cell lymphoma associated with Remicade and 6-MP at the time the black box warning was issued. This case is also distinguishable from Motus, where the treating physician testified unequivocally that he neglected to read the published warnings and did not rely on information from the drug representatives before prescribing the medication that allegedly induced the decedent to commit suicide. 385 F.3d at 661.

Summary judgment in favor of Centocor for lack of evidence of proximate causation is unwarranted.

Johnson and Johnson, Centocor's parent company, moves for summary judgment on the grounds that it has not been involved in the research, development, marketing or manufacture of Remicade, and that it has not controlled or dominated the activities of

Centocor to an extent that could give rise to parental liability for failure to warn. In support of these contentions, Johnson and Johnson has submitted a declaration by its Assistant Secretary, Lacey Elberg, executed on August 30, 2011. Plaintiffs respond that they have been unable to conduct discovery to explore the facts attested to by Ms. Elberg. Although in general a parent corporation is not liable for the acts of its subsidiaries, an exception may apply where the corporate veil may be pierced because "the corporate form would otherwise be misused to accomplish certain wrongful purposes." United States v. Bestfoods, 524 U.S. 51, 61-62 (1998). Discovery in this matter has been stayed since June 23, 2011, pursuant to the parties' stipulation. The parties agreed to stay discovery until after their mediation or the resolution of their motions for summary judgment, whichever occurred later. The parties stipulated that further discovery would be scheduled in the event that the case continued. Thus, Johnson and Johnson's motion for summary judgment is premature and the Court denies it without prejudice.

II. Motion for Reconsideration

As noted earlier, Plaintiffs move for reconsideration of the Court's prior order, granting summary judgment in favor of Abbott, TEVA, PAR and GSK, finding insufficient evidence of proximate causation with respect to Humira and 6-MP, based on the learned intermediary doctrine.

A district court may reconsider its grant of summary judgment under Federal Rule of Civil Procedure 59(e). Sch. Dist. No. 1J, Multnomah County, Or. v. ACandS, Inc., 5 F.3d 1255, 1262 (9th Cir. 1993).

Plaintiffs rely on the evidence discussed above, casting doubt on Dr. Rich's testimony that he was aware of the risk of hepatosplenic T-cell lymphoma in late 2005, as well as testimony by Dr. Rich that the Court did not discuss in its December 15, 2011 order. Specifically, the Court previously did not have the benefit of the Rosh Report, indicating that, as of February 2005, only one case report of hepatosplenic T-cell lymphoma had been published, and revealing the chronology of the medical publications on the risk of hepatosplenic T-cell lymphoma in combination therapy. Furthermore, the Court's prior order did not take full account of the ambiguities in Dr. Rich's testimony and the vagueness of his memory as to when he learned of the risk of hepatosplenic T-cell lymphoma. The Court reconsiders its December 15, 2011 order to ensure that it is supported in light of the full record of evidence concerning causation in connection with the three drugs at issue in this case. It would be unfair for Abbott, GSK, TEVA and PAR to escape the impact of certain evidence because it was only submitted in connection with Centocor and Johnson and Johnson's later motion for summary judgment. The Court will not issue inconsistent rulings simply because Defendants decided to move for summary judgment at different times. Accordingly, the Court reconsiders the merits of Abbott's, TEVA's, PAR's and GSK's motions for summary judgment. Docket Nos. 177, 179, 183 and 185.

Those Defendants moved for summary judgment on the grounds that Dr. Rich was aware early on of the risk of hepatosplenic T-cell lymphoma in adolescent and young adult patients taking Remicade with 6-MP. They relied on Dr. Rich's testimony that he knew, as of late 2005, of the risk posed by Remicade in

combination with immunosuppressants like 6-MP for young patients and that he considered those risks applicable to other TNF-blockers, such as Humira. For the reasons explained above, there is sufficient evidence to create a material dispute of fact as to whether Dr. Rich, in fact, knew about the risk in late 2005.

Abbott, TEVA and PAR argue that the newly considered evidence is not sufficient to change the outcome. They contend that the Rosh Report establishes that the first case report was published in February 2005 and an additional five cases were reported to the FDA's AERS through May 2006. They contend that this verifies Dr. Rich's testimony that he knew of the risk in late 2005, and that there is nothing to contradict it. However, there is no evidence indicating that Dr. Rich was apprised of cases of hepatosplenic T-cell lymphoma in young patients receiving concomitant Remicade and immunosuppressive therapy at the same time that they were being reported to AERS. Instead, the evidence indicates that Dr. Rich learned of these cases through the medical literature and the FDA black box warning. When Dr. Rich testified that he may have learned of two different cases from a colleague in the East Bay and a colleague from Atlanta, he did not recall that those conversations occurred before Maxx's diagnosis with hepatosplenic T-cell lymphoma. Thus, the evidence does not require summary adjudication that Dr. Rich learned of multiple cases of hepatosplenic T-cell lymphoma in late 2005 and therefore that a failure to warn of the risk did not cause Maxx harm.

Abbott, TEVA and PAR also argue that Plaintiffs cannot satisfy their burden to produce evidence of causation by simply challenging Dr. Rich's credibility as to when he learned about the

risk. Defendants contend that Plaintiffs made a strategic decision not to ask Dr. Rich directly whether a different warning would have caused him not to prescribe Humira or 6-MP. However, Plaintiffs are not limited to proving causation by relying on direct evidence. Rather, they rely on circumstantial evidence comprising Dr. Rich's course of conduct. Dr. Rich's testimony could support a jury finding that he did not learn of the risk of hepatosplenic T-cell lymphoma caused by combining Remicade and 6-MP in late 2005 but rather only in May 2006. Thereafter, he informed the Plaintiffs that Humira offered a better safety profile than Remicade and began prescribing Humira to Maxx on his relapse in November 2006. If a jury made such a finding, it could also rely on other testimony by Dr. Rich reasonably to infer that his knowledge of the risk influenced his decision to prescribe Humira, rather than Remicade, when Maxx relapsed in November 2006. Specifically, Dr. Rich testified that his awareness in November 2006 of the risk of hepatosplenic T-cell lymphoma in connection with Remicade and 6-MP informed his thinking about how to prescribe the medications. Accordingly, a jury could infer that knowledge of such a risk in connection with Humira would have informed his treatment decision as to combination therapy with that drug as well.

Plaintiffs have demonstrated that the Court's reconsideration of its prior ruling is warranted and they have produced sufficient evidence to raise a dispute of fact as to causation with respect to Humira and 6-MP. The Court's prior order granting summary judgment in favor of Abbott, TEVA and PAR is withdrawn and their motions are denied.

GSK submitted an opposition to Plaintiffs' motion for reconsideration separate from that submitted by Abbott, TEVA and PAR. In its opposition GSK adopted the arguments made by the three Defendants, but also argued that Plaintiffs cannot dispute that it ceased distribution of its 6-MP product, marketed as Purinethol, and sold its distribution rights for the product on July 1, 2003, before the risk of hepatosplenic T-cell lymphoma associated with 6-MP was reasonably scientifically knowable.

GSK first raised this issue in its March 2, 2011 motion for summary judgment. Plaintiff opposed the motion arguing that it was premature because further discovery was required to address the motion. On April 19, 2011, Court denied the motion without prejudice to allow for more discovery.

GSK raised the issue again in a footnote in its second motion for summary judgment, which otherwise relied on the issue of proximate causation. At the hearing, GSK requested that the Court look back at its March 2, 2011 motion for summary judgment and decide the merits of the issue. Plaintiffs have agreed to this request without the need for filing a further opposition to the motion. Therefore, the Court deems the motion resubmitted for consideration.

Plaintiffs have not disputed that there were no reports to AERS of hepatosplenic T-cell lymphoma associated with the use of Purinethol before July 1, 2003 and no such reports were published in medical or scientific literature by that date. Plaintiffs note only that the case report authored by M. Thayu and other researchers and published in February 2005 was received by the

journal for publication on May 18, 2003 and accepted for publication on October 15, 2004.

To succeed on their strict liability claim against GSK, Plaintiffs must produce evidence in support of its duty to warn. "Drug manufacturers need only warn of risks that are actually known or reasonably scientifically knowable." Carlin, 13 Cal. 4th at 1117 (emphasis in original). Although, necessarily, one occurrence of hepatosplenic T-cell lymphoma in connection with Purinethol was known by the authors of the case report before July 1, 2003, Plaintiffs have not presented evidence that the risk was actually known or should have been known by the scientific or medical communities of which GSK is a part. GSK is correct that information concerning the occurrence of hepatosplenic T-cell lymphoma in connection with Purinethol was not reported to AERS or discussed in the medical literature until after GSK ceased to distribute the drug. Furthermore, drug manufacturers are not required to warn of every conceivable adverse reaction. See id. at 1114-15 (noting that FDA regulations are relevant in a common law action for failure to warn and that a defendant could present evidence that, consistent with FDA regulations, it was not permitted to warn of the adverse effect because it was too speculative). Thus, GSK cannot be held strictly liable for failure to warn of the risk of hepatosplenic T-cell lymphoma associated with Purinethol.

Likewise, Plaintiffs' negligence claim requires them to prove that GSK "did not warn of a particular risk for reasons that fell below the acceptable standard of care; i.e., what a reasonably prudent manufacturer would have known and warned about." Id. at

1112. Plaintiffs have presented no evidence, expert or otherwise, indicating that a reasonable manufacturer would have been in a position to discover the case that Thayu and her co-authors reported, prior to July 1, 2003. Thus, Plaintiffs cannot prevail on their negligence claim against GSK.

GSK's motion for summary judgment on Plaintiffs' claims against it is granted.

CONCLUSION

The Court denies Centocor and Johnson and Johnson's joint motion for summary judgment. Docket No. 205. The Court grants Plaintiffs' motion for reconsideration. Docket No. 220. The Court's December 15, 2011 order is withdrawn and Abbott's, TEVA's and PAR's motions for summary judgment based on the learned intermediary doctrine are denied. Docket Nos. 177, 183 and 185. However, summary judgment in favor of GSK is granted on the grounds that there is insufficient evidence for a reasonable jury to find that, before July 1, 2003 when it discontinued distribution of Purinethol, it had a duty to warn of the risk of hepatosplenic T-cell lymphoma, as it argued in its March 2, 2011 motion. Docket No. 179. The remaining parties shall appear for a case management conference on August 8, 2012 at 2:00 pm, and shall submit a joint case management statement one week prior to the conference.

IT IS SO ORDERED.

Dated:

CLAUDIA WILKEN
United States District Judge